PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Anthony Peter MOLONEY

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SUBMISSION OF PRIORITY DOCUMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith is a certified copy of the priority document on which a claim to priority was made under 35 U.S.C. § 119. The Examiner is respectfully requested to acknowledge receipt of said priority document.

Respectfully submitted,

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Enclosures: **Certified copy of AUSTRALIA Patent Application No. 2002950744**

Date: January 20, 2004

Q76965

AUSTRALIA

Patent Office
Canberra

I, SMILJA DRAGOSAVLJEVIC, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. 2002950744 for a patent by MEDIHONEY PTY LTD as filed on 13 August 2002.

WITNESS my hand this
First day of September 2003

S. Dragosavljevic

SMILJA DRAGOSAVLJEVIC
TEAM LEADER EXAMINATION
SUPPORT AND SALES

Regulation 3.

Medihoney Pty Ltd

A U S T R A L I A

Patents Act 1990

PROVISIONAL SPECIFICATION

for the invention entitled:

"Composition"

The invention is described in the following statement:

COMPOSITION

FIELD OF THE INVENTION

The present invention relates to therapeutic compositions and in particular compositions including honey or honey derivatives.

BACKGROUND

Honey has been used as a natural remedy and therapeutic aid since ancient times and the anti-microbial properties of honey have long formed part of both folk and scientific knowledge. Applications for honey have been particularly directed to topical application for wounds, ulcers, burns and similar conditions. Honey has also been known to be used as a demulcent for use in the gastro-intestinal tract for soothing or allaying irritation of inflamed or abraded surfaces. Therapeutic benefits of honey use are manifested by a reduction in inflammation, swelling and pain; prevention and control of infection in a wound; reduction in malodour and exudate; assisted debriding of a wound and improved granulation and epilthelialisation of new tissue. These advantages help promote the rapid healing of a wound with minimal scarring.

Whilst these properties encourage the use of honey as a wound healing agent and provide a moist wound environment, regarded as beneficial to the healing of wounds, use has been mainly restricted to unmodified honey which has been applied in various forms of wound dressings and treatments. Application of honey directly presents difficulties arising from inherent properties of the material. Due to its relatively low viscosity and fluid nature plus natural "stickiness", honey tends to contaminate the local environment around a treatment region. The disadvantage of straight honey use is accentuated by the fact that honey at body temperature becomes reasonably fluid and migrates from a treatment site to further increase the chance of transfer to unintended areas. Use of honey can be time consuming,

messy and impractical.

Attempts have been made to address at least some of these problems by the use of extensive wound dressings which may form a physical barrier to honey migration and which may also be impregnated with honey. The use of these methods has added an extra layer of expense to treatment with honey and has provided variable success.

In using honey, the presence of wound fluid or exudate also dilutes the therapeutic agent exacerbating the problem of diminished contact time with the wound and diminished therapeutic efficacy. Attempts have also been made to address at least some of these problems by combination with other ingredients. Again the outcome has been variable in success rate. It is preferred, and possibly essential, that any combination be sterilised prior to use or commercial distribution. One common form of sterilisation requires gamma irradiation at a dose level that is toxic to microorganisms. Such a process is known to cause breakdown or undesirable changes in the matrix of the honey admixture.

While the therapeutic properties of honey are recognised and appreciated, there remains a problem with the practicality of using honey on wounds.

SUMMARY OF THE INVENTION

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

In one form although it need not be the only or indeed the broadest form the invention resides in a composition comprising honey or a honey derivative;

a fatty ester, wax or wax like compound and a surfactant.

The honey may be a single type of honey or may be a combination of one or more honeys. The one or more honeys may be selected for therapeutic properties which may include anti microbial activities. The honeys may be derived from one or more *leptospermum* species. In one embodiment, a honey derivative may be used. A honey derivative may be a modified form of honey formed by any one of various processes known to a skilled addressee.

Combinations of honey may include at least one honey with peroxide associated activity and at least one other honey with non peroxide associated activity. The honey or honeys may be selected on the basis of the levels of flavonoids and/or growth factors.

Honey is preferably present as at least 50% of the composition. Preferably the honey is present in the range of 70-90% of the composition and most preferably is present in a concentration of 80% of the composition. The percentage compositions in this specification are calculated on percentage weight/weight (% wt/wt).

The wax or wax like material preferably has a narrow melting point range around 40°C. Preferably the wax or wax like material has a melting point of 45°C or less. The wax like material may be Myristyl Myristate. Alternatively or additionally the wax or wax like material may be an emollient fatty ester or fatty alcohol. The Myristyl Myristate may be Crodamol MM.

The surfactant may be a low irritant, mild non ionic surfactant. The surfactant may be ethoxylated almond oil. The surfactant may alternatively comprise or include ethoxylated caster oil or ethoxylated evening primrose oil. The surfactant may be Crovol A70. The surfactant may be present in the range of 2-10%. Preferably the surfactant is present in the range of 3-7%. Most preferably the surfactant is

present as 5% of the ointment.

The fatty ester, wax or wax-like compound may be present in the ranges of 1-50% of the ointment. Most preferably the fatty ester or wax or wax-like compound is present in the range of 10-30%. In a preferred embodiment the fatty ester wax or wax-like compound is present as 15% of the ointment.

In a further aspect the invention resides in a method of producing a therapeutic honey ointment, the method comprising the steps of heating honey to a temperature which is below a temperature that will cause degradation, complete or partial, of at least one functional enzyme in honey;
combining a wax and a surfactant by heating and mixing;
cooling the mixture of wax and surfactant until it is similar to the temperature of the honey; and
combining the honey with the wax and surfactant. "Wax" in this context includes fatty esters and wax-like compounds.

The functional enzyme in honey may be glucose oxidase. The maximum temperature of the heated honey may be 45°C.

The wax and surfactant mixture may be heated to a temperature in the range of 50-60°C.

The wax and surfactant mixture may be mixed through the honey through high shear mixing until homogeneous, using caution to avoid overheating the mixture.

The method may include the step of sterilising the ointment. The ointment can be sterilised by applying one or more doses of gamma irradiation. The gamma irradiation may be provided at levels between 25-35kGy.

The method may further include the step of packaging the ointment for distribution.

In a further aspect the invention extends to a method of treating a subject by applying one or more doses of an ointment made according to the above method.

DETAILED DESCRIPTION

The present invention is directed to an easy to use, effective and stable honey based ointment. The ointment may be formed from a combination of honey or honey derivative, a surfactant and a wax or wax like component.

The honey component of the ointment may include a combination of one or more honeys selected for their therapeutic properties. The honeys may be derived from the Australian or New Zealand *Leptospermum* species. The honeys may include a combination of two or more honeys selected for differing but preferably complementary antibacterial action including those with peroxide and non peroxide associated activity. This combination may ensure a broad spectrum of anti-bacterial activity. Honeys may be selected on the basis of the presence of flavonoids which may act as an anti-oxidant resulting in inflammation reduction. Honeys may also be selected for the presence of growth factors which can assist with granulation, epithelialisation and the growth of new tissue to ensure a progressive and satisfactory healing process

The surfactant is preferably a low irritant, mild chemical. Preferably the surfactant is non ionic as, in general, this class of compounds is generally milder than ionic surfactants. A preferred surfactant is an ethoxylated triglyceride and in particular almond oil or a derivative thereof. Alternatively it is possible to substitute ethoxylated castor oil or ethoxylated evening primrose oil, preferably in non ionic form.

An example of a commercially available product is CROVOL A70 which is derived from sweet almond oil in an ethoxylated form. The international nomenclature for

cosmetic ingredients has allotted the name of PEG-60 almond glyceride to CROVOL A70. This product is a long chain ethoxylate and has been shown to have a very low tendency to irritation. CROVOL A70 has a chemical description as ethoxylated (70% by weight) sweet almond oil (CAS 124046-50-0) and may be obtained from Croda Australia, Wetherill Park, Sydney.

An additional essential ingredient is a fatty ester or wax. Preferably the fatty ester or wax has a relatively narrow melting range around 40°C and preferably in the range of 40-43°C. The preferred melting point is selected so that the ointment is substantially non-running at the body temperature of a patient which is in general around 37°C. In general however, it may be preferable to provide an ointment that maintains its viscosity up to 40°C to allow for temperature variation between species as the present invention is suitable for both veterinary and human use. One means of assessing whether the ointment is non-running is to place a sample on a slope, preferably at 45°, and demonstrate that the sample does not flow down the incline. The ointment sample may deform or bulge but preferably does not break and flow, except perhaps to an insignificant degree.

A preferred wax is Myristyl Myristate. Alternative ingredients may include any emollient fatty ester or fatty alcohol that satisfies the condition of having a relatively narrow melting range around 40°C. This temperature is above normal body temperature but it is also below the denaturing temperature of functional enzymes in honey which is generally accepted to be around 45°C. Most fatty esters have long hydro-carbon chains that are very stable. The ester group at the end of the molecule also provides a stable and non-reactive aspect to the compound, making it safe to use for this application.

An example of a commercially available source of Myristyl Myristate is Crodamol MM which is available from Croda Australia, Wetherill Park, Sydney.

In a preferred method of manufacture, honey is heated to a temperature that will

not degrade the functional enzymes, such as glucose oxidase, which occur in honey. Preferably this temperature is a maximum of 45°C. Separately, the wax and surfactant are heated while being mixed until both are fully melted. The temperature in this process may reach between 50-60°C. The wax/surfactant mixture is allowed to cool to the temperature of the honey at which time it is added to the honey with high shear mixing until homogenous. The mixing period may be relatively brief. It is important to avoid heating honey above the upper identified temperature as such a process may lead to degradation of functional enzymes with resulting diminishing of therapeutic effect.

The mixed ointment may then be allowed to cool and packaged for distribution.

Preferably the ointment is also sterilised particularly in relation to *Clostridium sp* spores and an associated reduction in bioburden levels. The preferred method of sterilisation is through the use of gamma irradiation, preferably at levels between 25-35kGy. One of the benefits of the present ointment is that it remains stable and homogenous after irradiation at these levels. The current formulation may be described as a fine wax dispersion in a honey matrix. The surfactant acts to keep the wax particles small and enables them to be suspended and dispersed throughout the honey. It has been found that some emulsifiers including lanolin are prone to denaturing or breakdown under irradiation making them unsuitable for use in the present composition.

The ointment may be formulated according to the following proportion:

Ingredient	Range (%wt/wt)
Honey	50 –97.9%
Myristyl Myristate	1-50%
Ethoxylated almond oil	2-15%

Preferably honey is present in the range of 75-83%. Myristyl Myristate may be the

range of 15-20% and ethoxylated almond oil may be present in the range of 2-7%.

The preferred embodiment has a composition of honey 80%, Myristyl Myristate 15% and ethoxylated almond oil 5%.

It is envisaged that the present ointment may be used for cosmetic rather than therapeutic purposes. In this case, selection of honeys with therapeutic characteristics is not essential. Honeys may be selected for cosmetic benefits such as providing a general moisturising action. Clearly, honeys may also be selected for the treatment of essentially aesthetic problems such as comedones or pimples. Selected honeys in these cases may be bacteriostatic.

Once produced, the ointment may be packaged and distributed in any suitable fashion. It may be dispensed into tubes. Alternatively it may be formed as part of a wound dressing by impregnation into a wound dressing material. The ointment may be packed into individual screw top containers or it may be delivered in sealed capsules or sachets for single use dispensing and treatment.

The ointment of the present invention may be applied in a wide range of situations and as already noted may be used in both human and veterinary medicine, as well as for human cosmetics. In its simplest form, the ointment may be applied topically to a lesion. The frequency of application may be varied to reflect the severity of the condition and the efficacy of the treatment. It is envisaged that an application rate of up to two to three times daily may be of benefit in some circumstances while application every 2-14 days may be suitable in other circumstances where the contact time is prolonged. The ointment is preferably of suitable viscosity that it may be molded or pressed into shape using finger pressure to adopt a configuration suitable for a lesion. That shape may be retained while the ointment is fixed in position by a support bandage or similar.

The ointment may be beneficially utilised in post surgical wounds, sinus wounds,

fistulas, burns, donor sites, infected wounds, pressure ulcers, venous ulcers, diabetic ulcers, trauma injuries, catheter exit sites, dental extraction sockets, fungating/malignant wounds, lesions and surgical procedures. This list is not comprehensive. Viscosity may be selected so that the ointment is suitable for filling wound cavities.

Clearly the present ointment may be applied to mucous membranes and may be dispensed into bodily cavities for treatment of mucous membranes. The ointment may be ingested in some circumstances for beneficial results. The composition of the ointment may be such that at body temperature, compared to room or storage temperature, it will soften and conform to a wound and surface to which it is applied and will remain in place for temperatures up to 37° and preferably up to 40°.

The present invention provides real benefits in the therapeutic use of honey. The use of 100% mixtures of honey is, as noted above, somewhat problematic. Additionally the use of honey in known methods can be quite irritating particularly to sensitive wounds. The present invention incorporates ingredients which are of natural origin and which do not have marked side effects such as mineral based products. The viscosity of the invention is such that it can be easily applied to a wide range of wounds some of which are painful to touch. As the surfactant can be a water soluble, vegetable derived emollient, the ointment can be easily washed off the body and can be irrigated out of body cavities. This advantage is of considerable significance as it provides easy clean-up of both patient and surrounding environments.

Manufacture of the ointment as described provides a product which can slowly dissolve over time in body fluid rather than be subject to immediate dilution and displacement by wound exudate. Additionally the ointment is suitable for internal use and for effective gamma irradiation st rilisation. The nature of the product makes it practical for bulk manufacture and relatively easy dispensing into

packages and containers.

The ingredients of the combination are known to be stable, inert, non irritating and safe to use in therapeutic application. Further the composition is such that a stable and homogenous mix of ingredients is achieved within the manufacturing temperature restrictions. The present invention reduces the problems associated with raw honey used in the treatment of wounds which occasionally causes stinging and sometimes painful sensations when applied to the wounds of patients. The ointment may be used for cosmetic purposes.

It is within the scope of the invention to add other ingredients known to a skilled addressee for various additional characteristics.

Throughout the specification the aim has been to describe the preferred embodiments of the invention without limiting the invention to any one embodiment or specific collection of features. Those of skill in the art will therefore appreciate that, in light of the instant disclosure, various modifications and changes can be made in the particular embodiments exemplified without departing from the scope of the present invention. All such modifications and changes are intended to be included within the scope of the disclosure.

DATED this 13th day of August 2001

Medihoney Pty Ltd

by DAVIES COLLISON CAVE

Patent Attorneys for the Applicants